## REMARKS

In the most recently received (final) Official Action, the Examiners have again provisionally rejected pending claims 11-15 under the judicially created doctrine of "obvious-type" double patenting. In addition, Examiners have once more rejected the presently pending claims under 35 U.S.C. 102(b) as being anticipated by the Blecha *et al.* PCT Publication, WO 96/32129.

In response, applicants have again amended independent claims 11 and 15 respectively; and enclose herewith a second replacment Terminal Disclaimer signed by the attorney of record. By the present claim amendments, the documentary enclosure and the discussion presented hereinafter, applicants believe they have overcome and obviated each basis for rejection stated by the Examiners in the most recently received (final) Official Action dated October 28th, 2004.

Applicants will now address and review each of the different substantive bases for rejection stated by the Examiners in the instant Official Action with regard to its legal requirements and the relevant factual circumstances. Initially, however, a summary of the present invention as defined by the presently pending claims is in order.

## I. Applicants' Claimed Invention

Applicants deem it essential to point out to the Examiners of record what their claimed invention precisely is in view of the current amendments to independent claims 11 and 15 as well as the particular bases of rejection stated by the Examiners of record in the instant Official Action.

Applicants' invention is claimed specifically as a "PR-39 derived oligopeptide family" and is defined by amended independent claims 11 and 15 respectively as a carefully defined class of specifically-sized amino acid residue sequences which are structurally analogous to native PR-39 molecule; whose individual members are all operative and functional; and which individually operate to cause a selective inhibition of protease-mediated degradation in-situ after their introduction intracellularly to a viable cell. In addition, several size-preferred embodiments of the membership constituting the PR-39 derived oligopeptide family are defined by dependent claims 12, 13 and 14 respectively as precisely structured amino acid residue sequences of specific lengths.

By the current amendments, it will be noted and appreciated that the wording of presently amended independent claims 11 and 15 recite specified ranges of size-limited structures as being operative and functional compositions of matter; and clearly define a membership of amino acid residue lengths which collectively encompasses the the

preferred 15, 11, and 8 amino acid residue length structures recited by dependent claims 12-14. Amended independent claims 11 and 15 respectively, therefore, delineate a circumscribed and size-limited membership which are structurally analogous to the amino acid residue sequence to be found at the N-terminal end of the native PR-39 molecule; and which are operative, functionally specific, and unique as a family of short-length oligopeptides.

In addition, the commonly shared characteristics and properties of the PR-39 derived oligopeptide family are overtly stated and individually set forth as operative elements and specific structural limitations by currently amended independent claims 11 and 15 respectively. Thus, amended independent claim 11 and claim 15 each requires that the individual PR-39 derived oligopeptide family member present not less than seven separate and individual traits and attributes. These are:

(1) a peptide family which is operative and functional;

(2) a pharmacologically active peptide family which structurally is either less than 26 amino acid residues in length [claim 11] or less than 20 amino acid residues in size [claim 15];

(3) a pharmacologically active peptide family whose N-terminal amino acid residue sequence begins with Arg-Arg-Arg;

(4) a pharmacologically active peptide family which is an analog of the N-terminal end amino acid sequence of the native PR-39 molecule;

(5) a pharmacologically active peptide family which operates to selectively alter the proteolytic degradation activity of proteasomes in-situ;

(6) a pharmacologically active peptide family operative to interact in-situ with at least the $\alpha 7$ subunit of such proteasomes as are present within the cytoplasm of the cell; and

(7) a pharmacologically active peptide family operative selectively to alter the proteolytic degradation activity of said proteasomes having an interacting $\alpha 7$ subunit such that the proteolytic degradation mediated by said proteasomes against at least one peptide selected from the group consisting of IκBα and HIF-1α becomes inhibited without substantially altering other proteolytic degradation mediated by said proteasomes.

It will be noted and appreciated also by the Examiners that currently amended independent claims 11 and 15 respectively set forth a precise structural recitation of the requisite elements and limitations comprising the minimal component parts of an operative and functional subject matter as a whole; and that the entirety of the claim language as recited - rather than any fraction or portion - constitutes and specifies the requisite elements and particular limitations of applicants' claimed invention.

II. The Obvious-Type Double Patenting Rejection

The Examiners have again provisionally rejected claims 11-15 under the judicially created doctrine of "obvious-type" double patenting over claims 11-14 of co-pending U.S. Application Serial No. 10/391,155 (US2004/0009463). Nevertheless, as the Examiners' have themselves noted (at pages 2-4 of the final Official Action), a timely filed Terminal Disclaimer in compliance with 37 C.F.R. 1.321(c) is legally sufficient and may be used to overcome a provisional rejection based on this non-statutory double patenting ground.

It will be noted that applicants did enclose such a Terminal Disclaimer and requisite fee payment as an attachment to the formal Response mailed August 10th, 2004. However, it appears that the original Terminal Disclaimer and fee payment is not presently to be found in the Examiner's file of record and appears to have gone astray.

In view of these circumstances, applicants now formally submit and enclose a second replacement Terminal Disclaimer document and a second fee payment of $65.00 [rate effective December 8th, 2004; FY2005] as required 37 C.F.R. 1.20(d). This second replacement Terminal Disclaimer document sets forth all the necessary binding commitments of 37 C.F.R.

1.321 and is signed by applicants' attorney of record in accordance with 37 C.F.R. 3.73(b).

Accordingly, the submission and filing of this second replacement Terminal Disclaimer and second requisite fee payment serves as a complete and appropriate response which overcomes entirely the stated basis for rejection. For this reason, applicants request that the Examiners reconsider their stated position and withdraw this ground of rejection against the presently pending claims.

III. The Rejection Under 35 U.S.C. 102(b)

The Examiners have rejected claims 11-15 under 35 U.S.C. 102(b) as anticipated by the Blecha *et al.* publication [PCT International Publication No. WO 96/32129]. Applicants note also that this PCT printed publication is identical to the text of and claims the priority of U.S. Patent No. 5,830,993 - a prior art U.S. patent, which is already formally of record and constitutes a substantive part of the prosecution file history for this application.

The Examiners' view, as stated at page 4, middle through Page 6, middle of the instant Office Action, is that the Blecha *et al.* publication teaches the same truncated PR-39 peptides (e.g., PR-14 and PR-19) as the oligopeptides cited in claims 12, 13 or 14 (e.g., peptides comprising SEQ ID NO: 3, 4 or 5); and that PR-14 and PR-19 have the same structural features

as the claimed truncated oligopeptides, - e.g., have less than 26 amino acid residues, having N-terminal Arg-Arg-Arg, and having identical amino acid sequence to the N-terminal region of native PR-39 peptide. On this basis, the Examiners then conclude by stating ..."Thus, the properties of the claimed PR-39 oligopeptides such as inhibiting proteasome-mediated degradation, being pharmacologically active, or interacting with the α7 subunit of proteasomes in the cytoplasm of the cell would be expected for the peptides of PR-14 and PR-19, even though the cited properties are not indicated in the reference...."

The Examiners have also seen fit to provide applicants with a copy of the Feit *et al.* published paper entitled "Inherency in Patent Law" [*J. Pat. Trade. Off. Soc. 85(1)*: 5-21 (2003)]; and directed applicants' attention to the substantive content of this published article as documentary support for the Examiners' stated views and positions regarding the legal doctrine of "inherency" [Page 6 of the final Office Action].

In response, applicants respectfully submit and maintain that:

(i) The Examiners' stated view and position concerning the teachings and suggestions of the Blecha *et al.* publication constitute a selective dissection and distortion of the information actually presented by the reference;

(ii) The Examiners have picked and emphasized only carefully chosen

portions of the Blecha *et al.* publication while concurrently omitting, ignoring and evading from other essential points of information within the publication; and

(iii) The Examiners are legally in error as regards their application of the inherency doctrine to the presently pending claims with respect to the rejection under 35 U.S.C. 102(b).

Applicants will now address, evidence and demonstrate each of these failures and deficiencies.

A. Factual Summary Of The Blecha *et al.* Publication

1. The Blecha *et al.* publication explicitly discloses an attempt to synthesize peptide compositions of varying size and amino acid residue formulation in order to identify whether or not these synthesized peptide variants are operative and functional, and could be used to inhibit microbial growth and microbial infections [Page 1, lines 7-30]. The Blecha *et al.* publication states that six variant shorter length fractionated peptide structures loosely based on the original PR-39 peptide were experimentally synthesized and empirically tested for operability and function. The amino acid residue formulation of each variant peptide fraction which was experimentally evaluated is shown by Fig. 1 [Page 5, lines 31-35; Page 6, lines 1-15].

2. Each of these six variant Blecha *et al.* peptide fractions empirically evaluated had a different residue length and each had a different and individual amino acid residue formulation. Of these six, three of the synthesized peptide variants were: PR-15, a fifteen residue length peptide structure constituting a fraction of the amino acid residues found at the COOH-terminal end of the native PR-39 peptide molecule; PR-16, a peptide sequence containing only the sixteen amino acid residue to be found at position nos. 11-26 in the native PR-39 peptide structure; and PR-23, a peptide sequence of twenty three residue length and having only amino acid residues to be found at position nos. 4-26 in the native PR-39 peptide. Thus, as a visual inspection of SEQ ID NOS: 6, 5 and 3 respectively in the publication shows, none of the PR-15, PR-16 or PR-23 peptide structures contained an N-terminus sequence beginning with the amino acid resides "Arg-Arg-Arg".

3. Of the six experimental peptide fractions empirically evaluated, only three variant peptides had an amino acid residue sequence which began with the amino acid residues found at the N-terminal end of the native PR-39 molecule. The three shorter-length peptide structures are: the PR-14 peptide fraction (a 14 amino acid residue length), the PR-19 peptide fraction (a 19

amino acid residue length), and the PR-26 peptide fraction (a 26 amino acid residue length) of the native PR-39 molecule.

4. The Blecha *et al.* publication provides empirical data and experimental results only as to whether or not any of the six peptide variants were operative and functional for demonstrating the anti-microbial biological activity provided by the native PR-39 molecule. The publication expressly and overtly states the following:

(i) While PR-26 was operative and showed antibacterial activity against *E.* coli in the gel-overlay assay, the PR-14, PR-15, PR-16, PR-19, and PR-23 variants were not operative or functional and did not show any antibacterial activity [page 12, 19-22];

(ii) While PR-26 was operative and showed antibacterial activity in the lawn-spotting assay, the PR-14, PR-15, PR-16, PR-19, and PR-23 variants were not operative or functional and did not show any antibacterial activity [page 12, lines 23-29]; and

(iii) While PR-26 was operative and significantly reduced $O_2$ generation by intact neutrophils, the PR-14, PR-15, PR-16, PR-19, and PR-23 variants were not operative or functional and did not reduce $O_2$ generation by intact neutrophils [page 15, lines 15-33].

5. In particular, among the three variant peptides whose formulations began with the amino acid residues found at the N-terminal end of the native PR-39 molecule, the PR-14 and the PR-19 variant peptides were not operative or functional, and failed to retain and to show any anti-microbial activity whatsoever [Page 15, lines 27-29]. Equally important, Blecha *et al.* observed and explicitly reported that, among the six variant peptides synthesized and experimentally tested, only the PR-26 peptide structure was operative and demonstrated any anti-microbial activity similar to that of the native PR-39 molecule [Page 12, lines 18-35; Page 13, lines 1-47].

6. The disclosure of the Blecha *et al.* publication also recites in detail what are the direct teachings and true conclusions for their reported empirical data and experimental results. These teachings and conclusions are clearly stated at page 12, lines 30-35 and page 13, lines 1-4 of the publication:

(a) The COOH-terminus of the PR-39 structure does not contribute to antibacterial activity;

(b) The N-terminus of the PR-39 structure is not sufficient for antibacterial activity;

(c) The PR-26 peptide containing residue Nos. 1-26 of the original PR-39 structure structurally is the antibacterial domain; and

(d) A particular secondary peptide structure and conformation is

required to exist and be present in order that antibacterial activity exist, as shown by only the PR-26 peptide variant and the native PR-39 molecule.

7. The Blecha *et al.* publication also explicitly and repeatedly states that only one variant peptide structure, the PR-26 peptide variant, is operative and functional, and thus alone is biologically active for the specified goal and stated purpose of demonstrating anti-microbial activity. Thus, of all six variant peptides actually synthesized and experimentally tested by Blecha *et al.*, only the PR-26 peptide variant is said to be operative and useful via its demonstrated antibacterial properties [Page 13, lines 5-25]. The other five variant peptide structures, by being empirically shown to be inoperative and non-functional entities, demonstrably have no biological activity whatever; and are therefore deemed by Blecha *et al.* to be of no technical use or scientific value as such.

B. The Relevant Legal Standards

1. An anticipatory reference must describe the claimed subject matter with sufficient clarity and detail to establish that the subject matter existed in the prior art, and that such existence would be recognized by persons of ordinary skill in the filed of the invention [In re Spada, 15 U.S.P.Q.2d 1655 at

1657 (Fed. Cir. 1990)]. Anticipation, however, specifically requires that each element and every particular limitation set forth in the claim language be found, either expressly or inherently described, in a single prior art reference [Verdegaal Bros. Inc. v. Union Oil Co., 2 U.S.P.Q.2d 1051 at 1053 (Fed. Cir. 1987); Richardson v. Suzuki Motor Co., 9 U.S.P.Q.2d 1913 at 1920 (Fed. Cir. 1989)].

If a single prior art reference does not expressly set forth an element or particular limitation of the claim, that reference still may anticipate if that element or limitation is "inherent" in its disclosure. However, in order factually to establish inherency, the extrinsic evidence provided by the prior art reference must make clear that the missing descriptive matter is necessarily present in the disclosure of the reference, and that the disclosed extrinsic evidence would be so recognized by persons of ordinary skill in the technical field [Continental Can Co. USA Inc. v. Monsanto Co., 20 U.S.P.Q.2d 1746 at 1749 (Fed. Cir. 1991)].

Anticipation can be found only if the prior art reference discloses, either expressly or under principles of inherency, every limitation and function recited by the claim in question [RCA Corp. v. Applied Digital Data Systems Inc., 221 USPQ 385 at 388 (Fed. Cir. 1984)]. The limitations which must be met by an anticipatory reference are those set forth in each statement of

function by the claims in question [In re Mott, 194 USPQ 305 at 307 (CCPA 1977)].

2. Equally important, to be legally competent and qualify as an anticipatory reference, the disclosure of the cited and applied reference must be "operable" - that is, the reference must be fully enabling in its technical content - such that the the public has sufficient knowledge of the presently claimed invention that they could make and use the claimed invention in a form operative to achieve its intended purpose [In re Hoeksema, 158 USPQ 596 (CCPA 1968; In re Donohue, 226 USPQ 619 (Fed. Cir. 1985)]. Also, a reference is legally presumed to be operable until there is a evidentiary showing that are sufficient and adequate facts which demonstrate that the technical content of the reference is inoperable. The burden of providing such an evidentiary showing, however, lies upon the applicant disputing the operability of the cited and applied reference [In re Sasse, 207 USPQ 107 (CCPA 1980); In re Wiggins, 179 USPQ 421 (CCPA 1971)].

Furthermore, the substantive disclosure of the anticipatory prior art reference must be so informative as to place one of ordinary skill in true possession of the claimed invention [Akzo N.V. v. U.S. International Trade Commission, 1 USPQ2d 1241 at 1245 (Fed. Cir. 1986); In re Wilder, 166 USPQ 545, 548 (CCPA 1970)]. The quality and quantity of knowledge and

understanding to be derived from the prior art publication must be sufficient to allow those skilled in the art or science to understand the nature and actual operation of the invention as claimed [Seymour v. Osborn, 78 US 516 at 555 (U.S. Sup. Ct. 1870)].

3. When relying upon the theory of inherency as the basis for rejecting a claim under 35 U.S.C. 102, the Examiners must provide adequate facts and/or technical reasoning to reasonably support any determination that the allegedly inherent characteristic necessarily flows from the teachings of the prior art reference [In re King, 231 USPQ 136 (Fed. Cir. 1986); W.L. Gore & Associates v. Garlock Inc., 220 USPQ 303 (Fed. Cir. 1983)]. In every instance, therefore, if an element or particular limitation recited by a claim is said to be inherently disclosed by a prior art reference, that element or limitation must be necessarily present within the reference in such an operative degree that a person of ordinary skill would clearly recognize its presence [Crown Operations Intl. Ltd. v. Solutia Inc., 62 U.S.P.Q.2d 1917 at 1921 (Fed. Cir. 2002); In re Robertson, 49 U.S.P.Q.2d 1949 at 1950-51 (Fed. Cir. 1999)].

It is also incumbent upon the Examiner of record to identify wherein each and every facet of the claimed invention is disclosed within the applied reference [Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick,

221 USPQ 481 (Fed. Cir. 1984)]. However, if the Examiner fails to provide such facts or evidence, he has failed to discharge his legal burden; and there is an insufficient basis to support any view that the claimed characteristic necessarily flows from or intrinsically exists within the prior art reference. Under these failed circumstances, any view or position that the claims in question are inherently anticipated is completely erroneous, factually unjustified, and legally unsupportable [In re Levy, 17 USPQ2d 1461 at 1464 (BPAI 1990)].

C. The Blecha *et al.* Reference Presents Negative Data & Negative Results

As set forth within the cited and applied reference, the five failed variant peptides synthesized by Blecha *et al.* are inoperative and non-functional structures; and they serve merely as laboratory test models and analytical workpieces in a prepared experimental program to identify what constitutes the anti-microbial domain and where the anti-microbial domain is to be found within the native PR-39 molecule. Also, by the express statements of the authors themselves, no scientific worth or value is afforded to any of the five failed peptide variants because they provide only negative data and negative results. Precisely for this reason, they are deemed by Blecha *et al.* to be solely and exclusively experimental tools by which to elucidate the mechanism of anti-microbial killing activity within the native PR-39 molecule.

Accordingly, for each of the five failed fractional peptide variants and the PR-14 and PR-19 fractional variants in particular which empirically failed to show any anti-microbial activity, the consequence of their demonstrated failure to show biological activity causes them to share a common status as follows:

(i) Each failed variant peptide sequence synthesized by Blecha *et al.* is and remains merely an inoperative and non-functional scientific curiosity having no scientific or technical value;

(ii) Each failed variant peptide sequence synthesized by Blecha *et al.* is merely a laboratory model and analytical tool suitable only as a recognized inoperative and non-functional workpiece for comparison purposes in further experimental efforts; and

(iii) Each failed variant peptide sequence synthesized by Blecha *et al.* is and remains an inoperative and non-functional substance which as been empirically demonstrated to be without any known utility owing to the absence of having any biological activity.

D. The Blecha *et al.* Publication Discloses Inoperative And Non-Functional Peptide Structures

1. Among the three variant peptides whose formulations begin with the amino acid residues found at the N-terminal end of the native PR-39 molecule, the PR-14 and the PR-19 variant peptides in particular

demonstrably failed to retain or reveal any anti-microbial activity whatsoever. Accordingly, there are no objective facts or probative evidence of any kind presented by the Blecha *et al.* publication which could offer or provide any reason or rationale whatsoever for inferring or imputing the existence of an operative or functional activity for these failed PR-14 and PR-19 variants. Unequivocally therefore, these PR-14 and PR-19 variant peptides are inoperative and non-functional compositions and structures, precisely because the reference itself empirically tested them and reported a complete absence of operation or function for these particular variants.

2. Also, as disclosed by the Blecha *et al.* reference, only the PR-26 peptide variant - the synthesized 26 amino acid residue fraction - was empirically found to be biochemically active and thus operable for its intended purpose. All of the other five failed variants, of any length shorter than 26 amino acid residues, showed no anti-microbial activity whatsoever. Thus, all five failed variants collectively are demonstrably inoperable and non-functional as such, precisely because the reference itself empirically tested them and reported a complete absence of operation or function for these particular variants to achieve the Blecha *et al.* desired goal and purpose. On this factual basis therefore, there are no objective facts or probative evidence of any kind within the Blecha *et al.* publication which could support or

validate any explanation or justification for inferring or intrinsically imputing the existence of an operative status for any of these five failed variants.

E. The Blecha *et al.* Publication Is Not Legally Enabling

1. As a matter of black letter law, to be legally competent and qualify as an anticipatory reference, the disclosure of the Blecha *et al.* reference must be "operable" - that is, the empirical data and experimental results must be fully enabling in its technical content - such that the the public would have sufficient knowledge of applicants' claimed invention and then could make and use applicants' claimed invention operatively and functionally to achieve its intended purpose. Furthermore, the substantive disclosure of the Blecha *et al.* reference must be so informative as to place one of ordinary skill in true possession of the claimed invention; and the quality and quantity of knowledge and understanding to be derived from the Blecha *et al.* publication must be sufficient to allow those skilled in the art to understand the nature and actual operation of applicants' invention as presently claimed.

2. However, in direct opposition and in complete contradiction to the Examiners' view and position as stated in the instant Official Action - because the empirical data of Blecha *et al.* showed that all five failed variants collectively and the PR-14 and PR-19 peptide fractional variants in particular

were inoperable and non-functional as such - these shorter length peptides cannot reasonably or rationally be said to have any operable or functional value at all. At most, these short-length peptide structures could be logically and objectively be expected to be biochemically neutral and pharmacologically quiescent, given the empirical data and experimental results actually reported by Blecha *et al.*

3. It is thus abundantly clear that the Blecha *et al.* publication is not operable and thus is not a legally enabling reference as concerns the five failed variants collectively and the PR-14 and PR-19 peptide fractional variants in particular. Precisely because these shorter length peptides cannot reasonably or rationally be said to be operable or functional in any respect, the disclosure of the Blecha *et al.* reference is not and cannot be "operable" evidence or facts. Clearly, the empirical data and experimental results reported by the Blecha *et al.* publication are not enabling in technical content; the public does not have any operative knowledge of applicants' claimed invention; and the public cannot make and presently use applicants' claimed invention operatively and functionally, owing to the negative experimental data and negative results reported by Blecha *et al.* for the five failed peptide variants.

F. The Examiners' Stated Position Concerning Inherency Is Erroneous

The Examiners' stated view and position is thus erroneous in two respects: First, the Examiner's view stands in factual opposition and in direct contradiction to the reported inoperable and non-functional empirical data and reported results of the Blecha *et al* publication itself. The Examiners' position is thus a *non sequitur*, an unreasonable conclusion that does not logically flow from its underlying premises. In effect, the Examiners have put forward an unreasonable and irrational stance which does not have any factual or rational underpinnings to support it; and then compounded their primary error presupposing and then artificially engrafting the existence of positive activities and properties for failed peptide variants whose only known existence previously are as inoperative and non-functional quiescent substances.

Second, the Examiners' position is based on a factual incompetent and legally non-enabling publication which is cited and applied as an anticipatory reference under 35 U.S.C. 102(b). In essence, the Examiners have subjectively chosen to draw positive inferences about operative attributes of short length peptide structures using only a factually deficient and non-informative Blecha *et al.* Publication which presents primarily negative empirical data and which unequivocally demonstrate and reveal only that the PR-14 and PR-19 factional variants are inoperative peptide structures.

Moreover, rather than recognizing and accepting the inoperative Blecha *et al.* empirical evidence as being a non-enabling disclosure,, the Examiners have ignored and evaded from the the negative results actually presented and evaluated by the Blecha *et al.* publication; and instead created an artificial fiction and a self-generated facade based on the bizarre and unsupported theory that once a peptide structure is synthesized for experimental evaluation purposes, some intrinsic properties must somehow exist for the synthesized peptide fractions - even if the reference empirically shows the short-length variants to be inoperative and biochemically quiescent.

F. The Examiners Have Committed Prejudicial Legal Error

1. Via this distorted view and illogical position, the Examiners have not complied with the legal requirements and standards necessary to employ or apply the inherency doctrine. The Examiners do not and can not show any factual teaching or overt suggestion from the Blecha *et al.* publication which objectively meets the structural elements and limitations recited by the claims now pending. Furthermore, as a matter of adjudicated case law which is legally binding upon the Examiners, their rejection basis of inherent anticipation relies solely upon negative empirical data and inoperative

structures - a factual and legal basis which is impossible, insupportable, and erroneous.

2. Applicants and their undersigned attorney do not accept and expressly reject the Examiners' continuing attempt to impute inherency and to graft artificially any operative attribute or positive function to the failed Blecha *et al.* peptide variants. Applicants respectfully submit that the Examiners have apparently forgotten that the sole and exclusive source of such knowledge and information is the Specification text of the present application. Accordingly, the only true factual basis and source suggestion for such operative peptide structures, positive properties and functional traits comes from hindsight knowledge which the Examiners impermissibly derived from applicants' disclosure. In this manner, therefore, the Examiners have committed major prejudicial legal error.

It remains applicants' view and position that the Examiners' use of and reliance upon the inherency doctrine as a basis for rejection fails to meet the necessary minimal legal requirements and standards of anticipation under 35 U.S.C. 102(b) because of the multiple inoperative peptide structures legally render the Blecha *et al.* reference as being non-enabling; and, moreover, because the disclosure of the Blecha *et al.* reference is so blatantly deficient in operative descriptive information, applicants maintain

that the rationale employed by the Examiners as the underlying basis for rejection is purely speculative and is without any substantive evidentiary foundation or factual support as such.

Applicants further submit that the inherency doctrine may not be properly employed as a legal basis for rejection of the claims under the present circumstances. Applicants affirm and maintain that their position is amply demonstrated and fully supported by the absence of relevant supporting facts, pertinent information, useful knowledge, or data within the cited and applied reference, the Blecha *et al.* publication.

*In Sum*, applicants find the Examiners' stated views and conclusions to be factually inaccurate and legally erroneous with respect to applicants' claimed invention. The Examiners' stated reasons for using the inherency doctrine and for employing the Blecha *et al.* publication as a proper reference and rejection basis have been shown to be unsupportable, unjustified and erroneous in their entirety. Accordingly, for all these reasons, applicants respectfully request that the Examiners reconsider their stated position and withdraw this ground of rejection against the presently pending claims.

Finally, applicants have addressed each basis of rejection stated in the recently received final Official Action forthrightly and objectively. In applicants' view, each relevant issue or controversy has been evaluated, acted upon and resolved completely. For these reasons, applicants respectfully submit and affirm that amended claims 11-15 now pending are therefore now allowable.

In view of the above discussion and detailed review, applicants believe that this case is now in condition for allowance and reconsideration is respectfully requested. The Examiners are invited to call applicants' undersigned attorney should they feel that such a telephone call would further the prosecution of the present application.

Respectfully submitted,

MICHAEL SIMONS
YOUHE GAO

Date: Dec. 23, 2004 By: _____

David Prashker
Registration Number 29, 693
Attorney for applicants
P.O. Box 5387
Magnolia, Massachusetts 01930
Tel: (978) 525-3794